

## Comparison of Mean Vitamin B12 Levels Among Patients with Mild To Moderate and Severe Depression, Using Hamilton Depression Rating Scale

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### ABSTRACT

**Objective:** To assess vitamin B12 deficiency and compare mean levels among patients with mild to moderate, and severe depression, using Hamilton Depression Rating Scale.

**Study Design:** Analytical cross-sectional study.

**Place and Duration of Study:** Armed Forces Institute of Mental Health (AFIMH), Rawalpindi, Pakistan, from Aug to Mar 2021.

**Methodology:** A total of 260 patients with diagnosed clinical depression with intensity ranging from mild to moderate, and severe, as per Hamilton Depression Rating (HAM-D) Scale, were included in this study. Patients were enrolled from the Outpatient Department of AFIMH and Depression Severity Scores (HAM-D score) and serum vitamin B12 levels were recorded for all participants.

**Results:** The average age of participants was 42.37±12.55 years. There were 105(40.38%) male and 155(59.62%) female patients. Out of 260 patients with depression, 185(71.15%) had mild to moderate depression and 75(28.85%) had severe depression. Frequency of vitamin B12 deficiency among patients with depression was 186(71.54%) while mean vitamin B12 levels were significantly higher in patients with severe depression as compared to patients with mild to moderate depression [245.53±63.98 vs. 173.39±51.97;  $p=0.0005$ ].

**Conclusion:** We found that patients with depressive disorders commonly have vitamin B12 deficiencies correlating with mild to moderate depressive symptoms.

**Keywords:** Depressive Disorder, HAM-D scale, Vitamin B12 deficiency

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### INTRODUCTION

Major Depressive Disorder is recognized as the most common psychiatric illness encountered globally with the highest global mortality rate.<sup>1</sup> About 350 million people suffer from depression.<sup>2</sup> While more than 800,000 people commit suicide due to which by the year 2030, it is expected to become the second most important leading cause of global morbidity.<sup>3</sup> In developed countries, 7 to 49% occurrence for depression has been reported while in Pakistan, it varies between 4.2 and 17%.<sup>4</sup> Depression is a multifactorial disorder, with biological (genetics, drugs, cardiovascular disease), psychological (neuroticism, negative self-image) and social (stress, negative life experiences, poverty) factors playing a role in its etiology,<sup>6</sup> with growing evidence supporting the association of nutritional factors as well.<sup>7</sup> Vitamin B complex, especially, has been reported to have an integral role in the regular functioning of the nervous

system with decreased serum vitamin B12 levels leading to changes in cell metabolism, resulting in neurological abnormalities such as depression, suicidal tendencies, decreased cognitive ability, psychosis and extreme agitating behavior.<sup>8</sup> In a two-years randomized clinical trial, improvement in depression symptoms and cognitive function in elderly people was noted when they were given regular Vitamin B12 and folic acid supplements( $p=0.032$ ).<sup>9</sup> In another randomized controlled trial, at the end of three months, all patients in the treatment group showed a 20% improvement in depression symptoms, as compared to only 69% of the patients in the control arm, who showed a 20% improvement in their depression symptoms ( $p<0.001$ ).<sup>10</sup> While the relationship between vitamin B12 levels and depression exists, the evidence is weak, therefore, this study aimed to investigate the relationship between serum vitamin B12 levels and different severities of depression to enable risk stratification and management to be planned accordingly.

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**METHODOLOGY**

This cross-sectional study was conducted from 31st August 2020 to 2nd March 2021, at the Outpatient Department of Armed Forces Institute of Mental Health (AFIMH), Rawalpindi, Pakistan, after gaining approval from the ethical review board vide letter no. 220/Adm, dated 15 February 2023. Our sample size was calculated by using WHO sample size calculator, where frequency of vitamin B12 deficiency was set as 22% among patients with depression.<sup>11,12</sup> We enrolled our sample by using nonprobability consecutive sampling.

**Inclusion Criteria:** Patients of either gender, with age ranging from 18 to 70 years, diagnosed with depressive disorder as per the Diagnostic and Statistical Manual of Mental Disorders (DSM) V, with both mild to moderate and severe depression and having either first depressive episode or recurrent depressive episodes were included.

**Exclusion Criteria:** Patients taking prescribed vitamin B12 supplements or having taken B12 supplements in the last three months, medical conditions associated with vitamin B12 deficiency, including pernicious anemia, atrophic gastritis, Crohn’s disease, celiac disease, immune disorders, such as, Grave’s disease and systemic lupus erythematosus, or patients taking medications which interfere with vitamin B12 absorption, such as, proton pump inhibitors, H2 receptor blockers and metformin, were excluded.

Informed, written consent was taken from the patients, and their age, gender, marital status, ethnicity, and socioeconomic status were recorded after which they were asked to fill out the Urdu version of the HAM-D scale and their scores were calculated. Depression severity scores were awarded out of a total of 50. The severity was categorized into 2 groups: Mild to Moderate Depression (Score 0-18) and Severe Depression (Score >18). Blood samples were collected, and vitamin B12 levels were assessed on ADIVA CENTARUX XP -2 at Armed Forces Institute of Pathology (AFIP), Rawalpindi. Individuals with vitamin B12 levels less than 150 pmol/L (203 pg/ml) were considered as having a vitamin B12 deficiency. Statistical Package for Social Sciences (SPSS) version 25 was used to analyze the recorded data. Gender, marital status and mild to moderate and severe depression as well as educational status were presented as frequency and percentage. Vitamin B12 levels and HAM-D scores of all participants were presented as mean and standard deviation (SD). In

order to compare the mean vitamin B12 levels between the two groups of patients, independent sample t-test was applied along with chi-square test where a *p*-value of <0.05 was considered to be significant.

**RESULT**

A total of two hundred and sixty (n=260) patients were included, with mean age 42.37±12.55 years (range 18 – 65). The majority of our patients were males 155(59.62%) and married 210(81.00%). Most patients 125(48.07%) had middle level to matric education. The mean duration of depression was 12.29+2.56 years while mean vitamin B12 levels were 194.20+64.4 pmol/L. Out of 260 patients with depression, 185(71.15%) had mild to moderate depression and 75(28.85%) had severe depression. Further clinical and demographic characteristics of our sample population are shown in Table-I.

**Table-I: Demographic and Clinical Characteristics of Patients (n=260)**

Variable	Mean ± SD	
Age (Years)	4.37 +12.55	
Duration of Depression (years)	12.29 + 2.56	
Vitamin B-12 (pmol/L)	194.20 +64.4	
Variable	n (%)	
Gender	Male	105(40.38%)
	Female	155(59.6%)
Marital Status	Married	213(81.92%)
	Unmarried	47(18.04%)
Education	Illiterate	50 (19.23%)
	Middle to Matric	125 (48.07%)
	Intermediate	60 (23.08%)
	Bachelor’s or above	25 (9.62%)
Severity of Depression	Severe	75(28.85%)
	Mild to Moderate	195(71.15%)
Vitamin B12 Deficiencies	Yes	186(71.54%)
	No	74(28.46%)

Mean vitamin B12 levels were significantly high in patients with severe depression as compared to patients with mild to moderate depression [245.53±63.98 vs. 173.39±51.97; *p*< 0.001], as shown in detail in Table-II.

**Table-II: Comparison of Vitamin B12 Levels Among Patients with Depression (n=260)**

Parameters	Depression		<i>p</i> -value (<0.05)
	Mild to moderate (n=175)	Severe (n=75)	
Vitamin B12 Levels	173.39±51.97	245.53±63.98	< 0.001

## Comparison of Mean Vitamin B12 Levels Among Patients

Mean vitamin B12 level was found to be significantly higher in patients with severe depressive symptoms as compared to patients with mild to moderate depressive symptoms, after controlling the effect of age, gender, and marital status, as shown in Table-III.

the prevalence of deficiency was 53.6%.<sup>17</sup> According to another study, up to 31% of patients with depression had low serum vitamin B levels.<sup>18</sup> but it was also observed that increased vitamin B levels were likely to be related to a better prognosis for patients.<sup>19,20</sup> According to one study, depression may raise a

**Table-III: Comparison of Mean Vitamin B12 Level Between Categories of Depression as compared by Age, Gender, and Marital Status (n=260)**

Parameters		Depression	Vitamin B12 Level (Mean± SD)	p-value (<0.05)
Age (years)	< 40	Mild to moderate (n=195)	179.40±42.51	0.005
		Severe (n=75)	234.44 60.75	
	≥ 40	Mild to moderate (n=195)	168.17 +58.59	0.004
		Severe (n=75)	262.17+ 66.10	
Gender	Male	Mild to moderate (n=195)	172.1 +44.16	< 0.001
		Severe (n=75)	212.8+ 39.94	
	Female	Mild to moderate (n=195)	174.2 +56.70	0.003
		Severe (n=75)	267.3 +67.91	
Marital Status	Unmarried	Mild to moderate (n=195)	176.29 +55.56	< 0.001
		Severe (n=75)	252.73 +70.40	
	Married	Mild to moderate (n=195)	156.41 +9.09	< 0.001
		Severe (n=75)	225.75 +35.96	

### DISCUSSION

In this study, 71.15% of patients had mild to moderate depression and 28.85% had severe depression. Mean vitamin B12 levels were significantly high in severe depressive cases as compared to mild to moderate depressive patients [ $p < 0.001$ ]. Vitamin B12 deficiency results commonly from abnormal absorption and insufficient dietary intake which leads to delayed DNA synthesis resulting in megaloblastic anemia along with psychiatric symptoms, due to which, despite the fact that the exact incidence of vitamin B12 deficiency in the general population remains unclear, the possibility of neuropsychiatric effects makes early detection by screening individuals at risk extremely valuable.<sup>13,14</sup> The average age of the patients in our study was 42.37±12.55 years with gender distribution being 40.38% male and 59.62% female, similar to another study, where the average age was 43.33±15.37 years for women and 44.24±15.48 years for men. In literature, depression is more frequently occurring among females (74.6%).<sup>14</sup> with the average age of patients presenting with depression to be 46.81 years.<sup>15</sup> Clinical research has revealed a relationship between serious depression and vitamin B12 deficiency where one study noted that 20% of patients with depression had low B12 levels.<sup>16</sup> while the frequency of vitamin B12 deficiency among patients with depression in our study was 71.54%, but another study in Nepal, using a cutoff level of 211 pg/ml for vitamin B12, found that

person's risk of having vitamin deficiencies, which may increase the severity of the depressive symptoms.<sup>21</sup> while another study reported that patients' symptoms were greatly reduced when they were given vitamin B12 and antidepressants.<sup>22</sup> One study found a positive correlation between symptoms of depression and vitamin B12 insufficiency among elderly patients.<sup>23</sup> similar to another study which showed that older persons with deficiency of vitamin D also had symptoms of depression,<sup>20</sup> which is somewhat similar to our findings where we found that patients ≤ 40 years of age had a somewhat higher rate of vitamin B12 deficiency but several other studies did not show a difference between the vitamin B12 levels of depression and control groups and no relationship between vitamin B12 deficiency and depression was found in these studies, which were primarily carried out in younger depressive patients.<sup>24,25</sup>

### LIMITATIONS OF STUDY

As a cross-sectional design, it cannot establish causality between vitamin B12 deficiency and depression severity, only associations at a single point in time. The study was conducted at a single military mental health institution in Pakistan, which may limit the generalizability of findings to broader civilian populations or different cultural contexts. Notably, the study lacks a healthy control group, making it impossible to determine whether the observed vitamin B12 deficiency rates are elevated compared to the general population.

### CONCLUSION

## Comparison of Mean Vitamin B12 Levels Among Patients

Our findings indicate that patients with depressive disorder commonly have vitamin B12 deficiencies. Clinicians need to be aware of the possibility of vitamin B12 deficiency in these patients and make efforts to identify and treat it to avoid neuropsychiatric dysfunction.

**Conflict of Interest:** None.

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### Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AMBS & SA: Data acquisition, data analysis, critical review, approval of the final version to be published.

AS & ZZZ: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MAK & RURG: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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